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| 10/030,436      | 03/21/2002  | Zoltan Greff         | 22096               | 6522             |

535 7590 03/14/2005

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EXAMINER

COLEMAN, BRENDA LIBBY

|          |              |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1624

DATE MAILED: 03/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/030,436

Applicant(s)

GREFF ET AL.

Examiner

Brenda L. Coleman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 12 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 28-54 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 28-35,38,40,41,49 and 50 is/are allowed.
- 6) ☒ Claim(s) 36,37,39,42-48 and 51-54 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Claims 28-54 are pending in the application.

This action is in response to applicant's amendments dated October 12, 2004. Claim 1-27 has been canceled and claims 28-54 are newly added.

### ***Response to Arguments***

Applicant's arguments filed October 12, 2004 have been fully considered with the following elect:

1. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 16-27 in the last office action, applicants' state that claims 16-27 have been cancelled and replaced with claims 47-54. The applicants filing of a Declaration under 37 C.F.R. 1.132 of Laszlo G. Harsing on December 14, 2004 is herein acknowledged. The applicants state that this Declaration provides both background information and physiological test data to establish that several represent compounds of the present Formula (I) have activity that enables their use to treat **a number** of neurodegenerative disorders including global cerebral ischemia, amyotrophic lateral sclerosis, stroke and cystic periventricular leukomalacia. While the compounds of the present Formula (I) may have been shown to have a positive effect in global cerebral ischemia, amyotrophic lateral sclerosis, stroke and cystic periventricular leukomalacia, this does not provide enablement for the treatment and/or prevention of the diseases and disorders as claimed herein. Evidence must demonstrate that AMPA antagonists and neurodegenerative diseases as a class are treatable.

It has been recited in claim 54, a method of treating neurodegenerative disorders. There is no such an agent, which can treat neurodegenerative disorders generally. That is because neurodegenerative disorders are extremely varied in origin and nature of effect. The origin and the nature of many neurodegenerative disorders such as Huntington's disease, Pick's disease, Frontotemporal dementia, Cerebro-Oculo-Facio-Skeletal (COFS) syndrome (cranofacial and skeletal abnormalities), Motor neuron disease (muscle weakness), Corticobasal ganglionic degeneration, Creutzfeldt-Jacob disease (fatal disease), Dementia with Lewy bodies, and Progressive supranuclear palsy Dementia are different one from the other. Many neurodegenerative disorders are untreatable to this day.

The symptoms and nature of these diseases are also different one from the other. It can be shown that many of these neurodegenerative disorders have different origin and nature of effect. Some neurodegenerative disorders are hereditary (Charcot-Marie-Tooth disease). Many neurodegenerative disorders vary in how they affect the body and its functions. Diseases such as Cerebral palsy, and Parkinson's disease affect the movement of the patient. Diseases such as Alzheimer's disease affect the memory of the patient.

Additionally, it is difficult to treat many of the disorders claimed herein. Instant claim language of claims 51 and 52 embraces disorders not only for treatment but also for the prevention, which is not remotely enabled. It is presumed in the prevention of the diseases and/or disorders claimed herein there is a way of identifying those people who may develop osteoporosis, etc. There is

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no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders claimed herein.

Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied upon are reasonably predictive of in vivo efficacy by those skilled in the art. See *In re Ruskin*, 148 USPQ 221; *Ex parte Jovanovics*, 211 USPQ 907; MPEP 2164.05(a).

Patent Protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. *Genentech Inc. v. Novo Nordisk* 42 USPQ2d 1001.

Claims 47, 48 and 51-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

2. The applicant's amendments and arguments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejections labeled a), b), c), d), e), f), g), i), j), k), l) and m) of the office action, which are hereby **withdrawn**. However, with regards to the 35 U.S.C. § 112, second paragraph rejections labeled h) the applicant's amendments and remarks have been fully considered but they are not persuasive.

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h) The applicants' stated that it is believed that all claims now presented are clear and definite and in full compliance with the requirements of that section of the statute. However, claim 24, which corresponds to newly added claims 47, 49, 51 and 53 are each pharmaceutical compositions of Formula (I) where the only difference is a statement of intended use in the preamble of the claim. Each claim is a compound of Formula (I) and a pharmaceutically acceptable inert carrier. Thus, as stated in the last office action with respect to canceled claim 24, newly added claims 47, 51 and 53 are substantial duplicates of claim 49 as the only difference is a statement of intended use, which is not given material weight. Note In re Tuominen 213 USPQ 89.

Claims 47, 51 and 53 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record and stated above.

3. The applicant's amendments and arguments are sufficient to overcome the 35 U.S.C. § 101 rejection of claim 26, labeled paragraph 4) of the last office action, which is hereby **withdrawn**.

4. The applicants' amendments, arguments and showing of unexpected results in the specification as originally filed of the compounds of the instant invention are sufficient to overcome the 35 U.S.C. § 103, obviousness rejections

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labeled paragraphs 5 and 6 of the last office action, which are hereby  
**withdrawn.**

In view of the amendment dated October 12, 2004, the following new  
grounds of rejection apply:

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

5. Claims 36, 37, 39 and 42-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a) Claim 36 is vague and indefinite in that it is not known what is meant by the nomenclature of the species where there is nothing between the hyphens, i.e. 7-acetyl- -5-(4-amino-3-methyl-phenyl)-7,8-dihydro-8-methyl- -9H-1,3- -dioxolo[4,5-h][2,3]benzodiazepine, emphasis added.

b) Claim 37 is vague and indefinite in that it is not known what is meant by the nomenclature of the species where there is nothing between the hyphens, i.e. 5-(3-methyl-4-amino-phenyl)-7-propionyl-7, 8-dihydro-8- -methyl-9H-1, 3-dioxolo[4,5-h][2,3]benzodiazepine (compound 1), 5-(4-amino-3-methyl-phenyl)-7-(N-cyclopropyl-carbamyl)-7,8-dihydro-8-methyl-9H- -1,3-dioxolo[4,5-h][2,3]benzodiazepine (compound 2), 5-(4-amino-3-

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methyl-phenyl)-7-(N-methoxy-carbamyl)-7,8-dihydro-8-methyl-9H-1,3-dioxolo[4,5-h][2,3]benzodiazepine (compound 3), 5-(4-amino-3-methyl-phenyl)-7-(N-methyl-carbamyl)-7,8-dihydro-8-methyl-9H-1,3-dioxolo[4,5-h][2,3]benzodiazepine (compound 4), 5-(4-amino-3-methyl-phenyl)-7-acetyl-8-cyano-7,8-dihydro-8-methyl-9H-1,3-dioxolo[4,5-h][2,3]benzodiazepine (compound 5) and 5-(4-amino-3-methyl-phenyl)-8-cyano-7-propionyl-7,8-dihydro-8-methyl-9H-1,3-dioxolo[4,5-h][2,3]benzodiazepine (compound 6), emphasis added.

c) Claim 39 is vague and indefinite in that it is not known what is meant by the nomenclature of the species where there is nothing between the hyphens, i.e. 7-(N-cyclopropyl-carbamyl)-5-(4-amino-3-methyl-phenyl)-8-methyl-7H-1,3-dioxolo[4,5-h][2,3]benzodiazepine (compound 2), emphasis added.

d) Claim 42 is vague and indefinite in that it is not known what is meant by the nomenclature of formula (III) where there is nothing between the hyphens, i.e. 8-formyl-5-(3-methyl-4-amino-phenyl)-9H-1,3-dioxolo[4,5-h][2,3]benzodiazepine (pages 13-14 of the amendment filed October 12, 2004), emphasis added.

e) Claim 42 is vague and indefinite in that it is not known what is meant by the nomenclature of formula (II) where there is nothing between



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the hyphens, i.e. 8-methyl-5-(4-nitro-3-methyl-phenyl)-9H-1,3- -

dioxolo[4,5-h] [2,3]benzodiazepine (page 14 of the amendment filed October 12, 2004), emphasis added.

f) Claim 42 is vague and indefinite in that it is not known what is meant by the nomenclature of formula (IV) where there is nothing between the hyphens or the "j", i.e. 5-(3-methyl-4-nitro-phenyl)- -9H-1,3-

dioxolo[4,5-h]**[2,3]**benzodiazepine-8-carboxylic acid (page 15 of the amendment filed October 12, 2004), emphasis added.

g) Claim 42 is vague and indefinite in that it is not known what is meant by the nomenclature of formula (III) where there is nothing between the hyphens or the "j", i.e. 8-formyl-5-(3-methyl-4-nitro-phenyl)-9H-1,3- -

dioxolo[4,5-h]**[2,3]**benzodiazepine (page 15 of the amendment filed October 12, 2004), emphasis added.

h) Claim 42 is vague and indefinite in that it is not known what is meant by R' in the process labeled e). It is believed that the applicants intended R<sup>1</sup>.

i) Claim 42 is vague and indefinite in that it is not known what is meant by C8-N7 double bond. It is believed that the applicants intended C<sup>8</sup>-N<sup>7</sup>.

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- j) Claim 42 is vague and indefinite in that it is not known what is meant by Formula (X1I) where numeral 1 is being used instead of a capital I.
- k) Claim 43 is vague and indefinite in that it is not known what is meant by Formula (X1) and (X11) where numeral 1 is being used instead of a capital I.
- l) Claim 44 is vague and indefinite in that it is not known what is meant by stannous(11)chloride where numeral 1 is being used instead of a capital I.
- m) Claim 46 is vague and indefinite in that it is not known what is meant by stannous(11)chloride where numeral 1 is being used instead of a capital I.

***Allowable Subject Matter***

6. Claims 28-35, 38, 40, 41, 49 and 50 allowed. None of the prior art of record or a search in the pertinent art area teaches the compounds, compositions and method of use of the compounds of formula (I) as claimed herein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The

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fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Brenda L. Coleman  
Primary Examiner Art Unit 1624  
March 6, 2005